

REMARKS

Claims 1 to 9 and 21 to 27 are pending and are variously rejected under 35 U.S.C. §§ 102 and 112, second paragraph. Previously withdrawn claims 10 to 20 have been canceled by amendment herein, without prejudice or disclaimer. Claim 22 has been amended as shown above. No new matter has been added by way of these amendments and the entry thereof is respectfully requested.

Applicants acknowledge with appreciation that the rejections based on 35 U.S.C. § 112, written description and § 103 have been withdrawn.

Obviousness-Type Double Patenting

Claims 1-9 and 21-27 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-8 and 16-18 of U.S. Patent No. 6,638,752. (Office Action, page 3). Applicants submit the appropriate terminal disclaimer herewith.

Rejection Under 35 U.S.C. §112, First Paragraph, Written Description

Claim 22 remains rejected under 35 U.S.C. §112, first paragraph, as allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, the Office reiterates "the instant specification satisfies the written description requirement only with regards to genetically engineered bacteria that function as biodetectors. The rejected claim is drawn to bacteria that 'shelter' the biodetectors, i.e., the biodetectors are genetically engineered bacteria that are 'sheltered' within other bacteria. ... This embodiment, contrary to Applicant's assertion, does not meet the written description requirement." (Office Action, page 4).

Applicants traverse the rejection for the reasons of record. *See*, Response filed November 6, 2000. In particular, it is reiterated that the application as filed does in fact contemplate and describe living biodetectors "sheltered" within other living entities. Nonetheless, solely to advance prosecution, claim 22 has been amended as shown above, and, accordingly, this rejection has been obviated.

Rejection Under 35 U.S.C. §102(b)

All examined claims are rejected under 35 U.S.C. §102(b) as allegedly obvious over Karube & Nakanishi (1994) *Current Opin Biotech* 5:54-59 (hereinafter "Karube") in light of

Sleight. (Office Action, page 5). It is maintained that Karube teaches cells comprising biodetectors for the detection and analysis of specific substrates. In addition, Sleight is cited for allegedly teaching the processes and components involved in signal transduction and illustrates that the biodetector disclosed by Karube inherently possesses the properties of the claimed biodetectors. (Office Action, page 5).

Applicants traverse the rejection and supporting remarks.

In order to be an anticipatory reference, the reference cited by the Office must disclose each and every element of the claims, including each and every functional or biological limitation. *See, e.g., Hybritech v. Monoclonal Antibodies*, 231 USPQ 81 (Fed. Cir. 1986); M.P.E.P § 2173.05(g) Functional Limitations, Eighth Edition. Moreover, the single source must disclose all of the claimed elements arranged as in the claims. *See, e.g., Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913 (Fed. Cir. 1989). Simply put, the law requires identity as between the prior art disclosure and the invention. *See, e.g., Kalman v. Kimberly-Clark Corp.* 218 USPQ 781 (Fed. Cir. 1983), *cert. denied*, 484 US 1007 (1988). Further, to support an anticipation rejection based on inherency, the Office must provide factual and technical grounds establishing that the inherent feature necessarily flows from the teachings of the reference. *See, e.g., Ex parte Levy*, 17 USPQ2d 1461, 1464 (BPAI 1990). Inherency cannot be established by probabilities or possibilities. *See, e.g., Continental Ca Co. USA, Inc. v. Monsanto Co.* 20 USPQ2d 1746, 1749 (Fed. Cir. 1987). Thus, the references must teach all elements of the claims, explicitly or inherently, including functional limitations such as biological function.

The Examiner has repeatedly concluded that Karube in light of Sleight teaches the existence of biodetectors as claimed. In particular, the Examiner maintains that the fact that the Karube discloses genetically engineered cells that use light to detect the effect of metals and pesticides on cells creates a presumption that the cells have all the elements of Applicants' claimed biodetectors. Additionally, the Office maintains that Sleight's review of signal transduction pathways provides the elements absent for Karube.

The Examiner's conclusions are improperly based on incorrect interpretations of the claimed invention and incorrect interpretations of what the references actually teach. Moreover, these conclusions are entirely contradicted by the evidence of record. Thus, Applicants submit that the Office has not met its burden of establishing a *prima facie* case of anticipation because Karube in light of Sleight does not inherently or expressly disclose the required ligand-activated signal transduction pathway of the claimed biodetectors.

As a threshold matter, Applicants note that the claimed invention is not, as asserted by the Examiner, directed to biodetectors of any and all configuration. In fact, the claims clearly

recite that the signal-converting element of the claimed biodetectors must comprise an extracellular ligand-specific moiety that selectively recognizes a selected substance. Moreover, the signal-converting element must also include an intracellular component that is activated by the specific binding of the substance to the extracellular component. Thus, the claims are directed to biodetectors in which a ligand must specifically bind to an extracellular moiety that in turn activates the intracellular moiety of the signal-converting element. The ligand itself is not transported across the cell membrane.

In contrast to Applicants' claims, Karube does not disclose or suggest biodetectors that function via signal transduction pathways. Rather, Karube relates entirely to detection of substances that both (1) bind non-specifically to the cell and (2) actually cross the cell membrane (e.g., metals and pesticides). With regard to the first point, Applicants note that it is (and was) known by persons of ordinary skill in the field of signal transduction that metals and toxins bind non-specifically to the surface of a host cell, and are taken into the cell via ion channels or other non-specific entry mechanisms. (see, e.g., Monteilh-Zoller Abstract and internet printout from chembytes attached hereto). Plainly, the non-specific entry mechanisms disclosed in Karube are not the "extracellular ligand specific domain," as recited in the claims.

Moreover, Karube also fails to describe, expressly or inherently, biodetectors comprising an intracellular domain that is activated by specific binding of the ligand to the extracellular moiety. Instead, in Karube's detectors, the substance (*i.e.*, metal or pesticide) binds non-specifically and then is itself transported across the cell membrane. This is quite a different proposition from the claimed biodetectors in which the ligand binds specifically and binding triggers the activation of the intracellular domain. Simply put, Karube does not disclose, inherently or explicitly, biodetectors in which binding of a ligand activates a signal transduction pathway. Accordingly, this reference cannot anticipate the pending claims.

Furthermore, because Karube is entirely unrelated to signal transduction pathways, the disclosure cannot be properly viewed in light of Sleight, which relates entirely to signal transduction pathways, all of which are characterized by the fact that the ligand does not itself enter the cell.

Thus, it is plain that a biodetectors as claimed, are not disclosed in Karube, either alone or in light of general references regarding signal transduction pathways.

CONCLUSION

Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

If the Examiner notes any further matters that the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

Please direct all further communications in this application to:

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Date: December 22, 2003

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